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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,520	09/22/2003	Andre Stamm	107664.115 US8	5815

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EXAMINER
SHEIKH, HUMERA N

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,520	STAMM ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24,55-81,183-186,191,192 and 203-210* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,55-81,183-186,191,192 and 203-210* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response after Non-Final Office Action, Applicant's Arguments/Remarks and the request for extension of time (3 months), all filed 3/6/07 is acknowledged.

Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 are pending in this action. Claims 25-54, 82-182, 187-190 and 193-202 have previously been cancelled. No claims have been amended herein. Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 remain rejected.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtet *et al.* (US Pat. No. 4, 895,726) in view of Duclos *et al.* (U.S. Pat. No. 5,776,495).

The instant invention is drawn to a process for producing a fenofibrate composition comprising: (i) preparing a suspension comprising at least one hydrophilic polymer, and micronized fenofibrate; (ii) spraying the suspension onto inert carriers.

The instant invention is also drawn to a process for producing a fenofibrate composition comprising: (i) preparing an aqueous suspension comprising at least one hydrophilic polymer, at

least one surfactant and micronized fenofibrate; (ii) spraying the aqueous suspension onto inert carriers.

Curtet *et al.* ('726) teach a method for the preparation of a fenofibrate composition and the fenofibrate composition obtained therefrom comprising fenofibrate particles in combination with a solid surfactant, wherein the fenofibrate and solid surfactant have been co-micronized (see reference column 1, line 1 - col. 2, line 68); examples and claims. Curtet *et al.* teach an intimate mixture of co-micronized fenofibrate and a solid surfactant, wherein the mixture is converted to granules in the presence of water (col. 2, lines 5-20). The preferred surfactant taught is sodium lauryl-sulfate in a recommended amount of between 0.5% and 7% by weight (col. 1, lines 52-60). Curtet *et al.* teach overlapping amounts of fenofibrate and the hydrophilic polymer-polyvinylpyrrolidone, wherein the fenofibrate is present in an amount of 200 mg per therapeutic unit (col. 1, lines 50-51) and the polyvinylpyrrolidone is contained in an amount of 7 mg (col. 3, lines 21-32). The fenofibrate/solid surfactant mixture granules have a mean particle size of less than 15 μm (col. 1, lines 61-66). Filling, dispersing and flow-enhancing excipients can be added and include lactose, starch, polyvinylpyrrolidone and magnesium stearate (col. 1, line 67 – col. 2, line 4).

According to Curtet *et al.*, it is known that the micronization of an active principle is capable of improving the dissolution of the said active principle in vivo, and hence its bioavailability. It is also known that the addition of a surfactant excipient to a formulation of an active principle is capable of improving the absorption and consequently the bioavailability of the said active principle (col. 1, lines 28-34).

The fenofibrate composition can be presented in the form of gelatin capsules, which are especially useful in the oral treatment of hyperlipidemia and hypercholesterolemia (col. 1, lines 44-49).

Curtet *et al.* teach that the weight ratio of surfactant/fenofibrate will be between about 0.75/100 and 10.5/100 (col. 1, lines 59-60). Curtet *et al.* do not explicitly teach the claimed weight ratio of the fenofibrate/hydrophilic polymer & claimed surfactant/hydrophilic polymer weight ratio. Curtet *et al.* also do not teach the claimed fenofibrate and hydrophilic polymer amounts/ranges. However, Applicants have not demonstrated any unexpected or superior results attributable to the claimed weight ratio of the fenofibrate/polymer & surfactant/polymer, nor the amounts of fenofibrate and polymer claimed. Suitable or effective weight ratios of drug/polymer, surfactant/polymer and amounts ranges of drug/polymer could be determined by one of ordinary skill in the pharmaceutical art through routine or manipulative experimentation to obtain optimal results, as these are indeed variable parameters attainable within the art.

Curtet *et al.* do not expressly state a fenofibrate suspension, but rather a composition, wherein co-micronized granules are contained in the presence of water. However, it is well known in the art to incorporate a medicament, such as fenofibrate in combination with water and a surfactant to form a suspension.

In any event, **Duclos *et al.* ('495)** are relied upon for their teaching that drugs with poor solubility in water can be modified favorably by adjunction of non-ionic surfactants, solubilizing agents and that micronization of medicaments increases the external specific surface area and are convenient for pharmaceutical forms, such as suspensions. Duclos *et al.* also teach that adjunction of surfactants can increase the solubility of active components and thereby improve

the kinetics of resorption (see reference column 1, lines 18-37). Duclos *et al.* teach that poorly soluble active ingredients include fenofibrate (col. 5, line 6).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a suspension of micronized fenofibrate as taught by Duclos *et al.* within the fenofibrate composition of Curtet *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Duclos *et al.* teach micronization of medicaments in suitable forms such as suspensions, can be beneficial in increasing solubility of active components and thereby improving the kinetics of resorption and consequently, the bioavailability of active ingredients. The expected result would be an improved process for obtaining a bioavailable fenofibrate suspension formulation, which can be administered once a day.

Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtet *et al.* (US Pat. No. 4, 895,726) in view of Ikeda *et al.* (U.S. Pat. No. 5,952,356).

The instant invention is drawn to a process for producing a fenofibrate composition comprising: (i) preparing a suspension comprising at least one hydrophilic polymer, and micronized fenofibrate; (ii) spraying the suspension onto inert carriers.

The instant invention is also drawn to a process for producing a fenofibrate composition comprising: (i) preparing an aqueous suspension comprising at least one hydrophilic polymer, at least one surfactant and micronized fenofibrate; (ii) spraying the aqueous suspension onto inert carriers.

Curtet *et al.* ('726) teach a method for the preparation of a fenofibrate composition and the fenofibrate composition obtained therefrom comprising fenofibrate particles in combination with a solid surfactant, wherein the fenofibrate and solid surfactant have been co-micronized (see reference column 1, line 1 - col. 2, line 68); examples and claims. Curtet teach an intimate mixture of co-micronized fenofibrate and a solid surfactant, wherein the mixture is converted to granules in the presence of water (col. 2, lines 5-20). The preferred surfactant taught is sodium lauryl-sulfate in a recommended amount of between 0.5% and 7% by weight (col. 1, lines 52-60). Curtet teach overlapping amounts of fenofibrate and the hydrophilic polymer-polyvinylpyrrolidone, wherein the fenofibrate is present in an amount of 200 mg per therapeutic unit (col. 1, lines 50-51) and the polyvinylpyrrolidone is contained in an amount of 7 mg (col. 3, lines 21-32). The fenofibrate/solid surfactant mixture granules have a mean particle size of less than 15 μm (col. 1, lines 61-66). Filling, dispersing and flow-enhancing excipients can be added and include lactose, starch, polyvinylpyrrolidone and magnesium stearate (col. 1, line 67 – col. 2, line 4).

According to Curtet *et al.*, it is known that the micronization of an active principle is capable of improving the dissolution of the said active principle in vivo, and hence its bioavailability. It is also known that the addition of a surfactant excipient to a formulation of an active principle is capable of improving the absorption and consequently the bioavailability of the said active principle (col. 1, lines 28-34).

The fenofibrate composition can be presented in the form of gelatin capsules, which are especially useful in the oral treatment of hyperlipidemia and hypercholesterolemia (col. 1, lines 44-49).

Curtet *et al.* teach that the weight ratio of surfactant/fenofibrate will be between about 0.75/100 and 10.5/100 (col. 1, lines 59-60). Curtet *et al.* do not explicitly teach the claimed weight ratio of the fenofibrate/hydrophilic polymer & claimed surfactant/hydrophilic polymer weight ratio. Curtet *et al.* also do not teach the claimed fenofibrate and hydrophilic polymer amounts/ranges. However, Applicants have not demonstrated any unexpected or superior results attributable to the claimed weight ratio of the fenofibrate/polymer & surfactant/polymer, nor the amounts of fenofibrate and polymer claimed. Suitable or effective weight ratios of drug/polymer, surfactant/polymer and amounts ranges of drug/polymer could be determined by one of ordinary skill in the pharmaceutical art through routine or manipulative experimentation to obtain optimal results, as these are indeed variable parameters attainable within the art.

Curtet *et al.* do not expressly state a fenofibrate suspension, but rather a composition, wherein co-micronized granules are contained in the presence of water. However, it is well known in the art to incorporate a medicament, such as fenofibrate in combination with water and a surfactant to form a suspension.

In any event, **Ikeda *et al.* ('356)** are relied upon for their teaching of pharmaceutical compositions that include fibrate compounds, such as fenofibrate that have actions of lowering blood cholesterol levels and whereby the compositions can be in suitable forms, such as suspensions (see reference column 10, line 64 – col. 11, line 3); (col. 11, line 65 – col. 12, line 35); (col. 13, lines 51-58).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate fenofibrate pharmaceutical compositions in the form of

suspensions, such as taught by Ikeda *et al.* within the fenofibrate composition of Curtet *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Ikeda *et al.* teach pharmaceutical compositions comprising fenofibrate that are suitably in the form of suspensions and teach that such formulations are effective for lowering blood cholesterol levels in a patient. The expected result would be an enhanced fenofibrate suspension formulation and process for the beneficial for the treatment of elevated cholesterol levels.

Response to Arguments

Applicant's arguments filed 03/06/07 have been fully considered but they are not persuasive.

Rejection under 35 U.S.C. 103(a) over Curtet ('726) in view of Duclos ('495):

Applicant argued, "Curtet does not disclose or suggest any suspension of micronized fenofibrate. Curtet never teaches a solution of at least one polymer, and does not provide motivation to produce a solution containing at least one polymer. Curtet teaches away from a suspension and requires that the surfactant be in solid form. Duclos does not cure the deficiencies of Curtet. Duclos claims a process for preparing a solid dispersion. Duclos does not teach a suspension of micronized active ingredient, but a solution containing the active ingredient in dissolved form. The invention, in contrast, is directed to a suspension of fenofibrate in a micronized form. The claimed invention provides a suspension of active ingredient, which is an intermediate product which is used in the manufacture of a final composition having an improved dissolution."

Applicant's arguments have been considered, but were not persuasive. Applicants have not sufficiently established unexpected results, which would amply distinguish over the art of record, by their use of a suspension. The prior art initially recognizes and teaches a similar formulation as claimed, which utilizes the same components as that being claimed by the Applicant. Namely, Curtet teach an intimate mixture of co-micronized fenofibrate and a solid surfactant, wherein the mixture is converted to granules in the presence of water (col. 2, lines 5-20). Applicants have not established any patentable distinction over the reference teachings based on their use of a suspension of micronized fenofibrate. Suitable forms, including suspensions can be determined by one skilled in the art, based on the intended purpose or outcome. The claims, at present, remain generic enough to read on the reference teachings.

Rejection under 35 U.S.C. 103(a) over Curtet ('726) in view of Ikeda ('356):

Applicant argued, "Ikeda states no preference for any fibrate compound, nor provides working examples that use any type of fibrate. Suspensions are mentioned in a list of possible dosage forms. No preference is placed on suspensions. Moreover, Ikeda is non-analogous art."

Applicant's arguments have been considered, but were not persuasive. The secondary reference of Ikeda was relied upon for their general teaching of pharmaceutical compositions that include fibrate compounds, such as fenofibrate that have actions of lowering blood cholesterol levels and whereby the compositions can be in suitable forms, such as suspensions (see above). Applicant's argument that "no preference is given for any fibrate compound, nor of suspensions" was not persuasive since preferred as well as non-preferred teachings are considered in determining patentable subject matter. Applicant is reminded that a reference is not limited to

its' preferred embodiments, but is considered for what it discloses as a whole. Moreover, the reference recognizes the use of compositions that include fibrate compounds and also teaches forms, such as suspensions and thus the reference teachings are a positive suggestion in the art. In response to applicant's argument that Ikeda is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Ikeda clearly teaches compositions comprising fibrate compounds, whereby the formulations can be pharmaceutical suspensions, that are effective for lowering blood cholesterol levels in a patient.

The instant claims remain unpatentable over the cited art of record delineated above.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh

HUMERA N SHEIKH
PRIMARY EXAMINER

Primary Examiner

Art Unit 1615

May 18, 2007